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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/506,651	11/16/2004	Dimiter Stanchev Dimitrov	015280-458000US	3349

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EXAMINER

HUMPHREY, LOUISE WANG ZHIYING

ART UNIT	PAPER NUMBER
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1648

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	02/22/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No. 10/506,651	Applicant(s) DIMITROV ET AL.	
	Examiner Louise Humphrey, Ph.D.	Art Unit 1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 20 November 2006.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-84 is/are pending in the application.
- 4a) Of the above claim(s) 5-9, 11-49, 51-54 and 56-84 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-4, 10, 50 and 55 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 02 September 2004 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

The Office acknowledges the receipt of Applicant's election and Amendment, filed on 20 November 2006.

Election/Restriction

Applicant elects Group I, claims 1-4, 10, 50 and 55, with traverse. The traversal is on the grounds that Examiner has not demonstrated that the claims do not relate to a single general inventive concept. Applicant's traversal is not persuasive for the claimed invention lacks a special corresponding technical feature. As the Applicant indicated in the reply, the common technical feature of the inventions is a HIV gp120-gp41 fusion polypeptide wherein the carboxy-terminal end of gp120 is covalently linked through a peptide linker to the amino-terminal end of gp41. Such a composition is disclosed in US 2004/0109887 (effectively filed on 20 April 2001) as set forth below in the rejection under U.S.C. §103.

The restriction among the different products that may be used in the claimed methods is maintained. The requirement is still deemed proper and is therefore made FINAL.

Claims 1-84 are pending. Claims 5-9, 11-49, 51-54, and 56-84 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 20 November 2006.

Claims 1-4, 10, 50 and 55 are examined in the instant application.

Specification

Applicant is required to update the status (pending, allowed, etc.) of all parent or priority applications in the first line of the specification. The status of all citations of US filed applications in the specification should also be updated where appropriate.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. §103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1-3, 10, 50 and 55 are rejected under 35 U.S.C. §103(a) as being unpatentable over Wyatt *et al.* (US 2004/0109887, effective filing date 20 April 2001) in view of Rovinski *et al.* (US 5,866,320).

The instant invention is an antigenic composition comprising a human immunodeficiency virus (HIV) envelope glycoprotein 160 (gp160) having a gp120 subunit and a gp41 subunit wherein the carboxy-terminal end of gp120 is covalently linked through a peptide linker of at least 5 amino acids, to the amino-terminal end of gp41.

Wyatt *et al.* disclose an immunogenic composition containing a trans-membrane protein, including viral glycoproteins constructs derived from the primary R5 HIV-1 isolates. See Abstract. Covalently linked gp120-gp41 glycoproteins are created by replacing the arginines 508 and 511 with serines in a site-directed mutagenesis and

Art Unit: 1648

thereby disrupting the proteolytic cleavage site between gp120 and gp41. See page 13, ¶132. Wyatt *et al.* do not disclose a peptide linker of at least 5 amino acids.

Rovinski *et al.* suggest inserting an antigenic marker into a *gag* gene product, a *pol* gene product and an *env* gene product. See Abstract. The at least one-antigenic marker may have about 5 to about 100 amino acid residues, particularly about 10 to about 75 amino acid residues. The antigenic marker may comprise at least one antigenic epitope from another virus. The invention is illustrated, in one embodiment, by at least one antigenic epitope from tobacco mosaic virus (TMV) coat protein, specifically including an amino acid sequence AFDTRNRIIEVEN (SEQ ID NO: 1) or a portion, variation or mutant thereof capable of eliciting antibodies that recognize this sequence, or multiple copies, specifically from 1 to 4, of such amino acid sequence. See column 2, line 35-45.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the composition of Wyatt *et al.* by replacing the serine linker with a peptide linker that is an antigenic marker as suggested by Rovinski *et al.* The skilled artisan would have been motivated to do so because the antigenic marker allows one to differentiate between infection by HIV or another retrovirus such as non-infectious, retrovirus-like particle. Thus, the invention as a whole was clearly *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Art Unit: 1648

Claims 1-4, 10, 50 and 55 are rejected under 35 U.S.C. §103(a) as being unpatentable over Wyatt *et al.* (US 2004/0109887, effective filing date 20 April 2001) in view of Root *et al.* (US 5,635,599).

The instant invention is further limited to one of the peptide linkers of SEQ ID NO: 10-14.

The relevance of Wyatt *et al.* is set forth above. Wyatt *et al.* do not disclose the peptide linker of any of SEQ ID NO: 10-14. However, Root *et al.* disclose fusion proteins of N-helices and the C-helices of the trimer-of-hairpin structure of HIV gp41, separated by peptide linkers of GGSGG. See Abstract, ¶4 and Figure 11A and 11B. The claimed peptide linker sequences (SEQ ID NO:12, 13, 14), respectively, (GGSGG)₃, (GGSGG)₄, and (GGSGG)₅, are tandem repeats of the prior art peptide linker, GGSGG.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the composition of Wyatt *et al.* by replacing the serine linker with a tandem repeat of the GGSGG peptide linker as suggested by Root *et al.* The skilled artisan would have been motivated to do so to increase the flexibility of the linker, because glycine is the smallest nonpolar amino acid, in order to preserve and to stabilize the native conformation of the gp120-gp41 complex. There would have been a reasonable expectation of success, given the working examples of fusion proteins comprising the suggest peptide linkers, as suggested by Root *et al.* Thus, the invention as a whole was clearly *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Art Unit: 1648

Correspondence

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Louise Humphrey, Ph.D. whose telephone number is 571-272-5543. The examiner can normally be reached on Mon-Fri, 9:30 am - 5:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce Campell can be reached on 571-272-0974. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.



Jeffrey Parkin, Ph.D.
Primary Examiner
31 January 2007



Louise Humphrey, Ph.D.
Assistant Examiner